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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,500	11/14/2000	Christine Van Broeckhoven	B0192/7019	9967

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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,500	VAN BROECKHOVEN ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,20,25-27 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,20,25-27 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/21/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 21, 2004 has been entered.

Claims 1-10, 20, 25-27 and 29 are pending. All rejections not reiterated herein are hereby withdrawn. This action contains new/modified grounds of rejection and is made non-final.

2. The previous requirement for a new Oath/Declaration is withdrawn in view of the Oath/Declaration filed October 21, 2004.

Claim Objections

3. Claim 20 is objected because a claim to a product does not properly depend from a claim to a method in which that product may be used. (SEE MPEP 608.01(n)). It is noted that claim 7, from which claim 20 depends, is not drawn to a method of preparing nucleic acids and is not drawn to nucleic acids themselves, but rather is drawn to methods in which nucleic acids are identified. It is improper for a method which uses a product to depend from a method which identifies a product.

Response to Arguments:

The response does not specifically traverse this rejection. Rather, the response at page 11 states that claim 20 has been amended to clarify the identity of the probe as a cDNA encoded by the coding region/gene identified in the method of claim 7. However, claim 7 is not drawn to the actual coding region or gene but rather to a method for identifying a coding region or gene. A claim to a method of using a product does not properly depend from another method in which that product may be identified. Applicants attention is again directed to MPEP 608.01(n). As stated therein, "(T)he test as to whether a claim is a proper dependent claim is that it shall include every limitation of the claim from which it depends (35 U.S.C. 112, fourth paragraph) or in other words that it shall not conceivably be infringed by anything which would not also infringe the basic claim... On the other hand, if claim 1 recites a method of making a specified product, a claim to the product set forth in claim 1 would not be a proper dependent claim since it is conceivable that the product claim can be infringed without infringing the base method claim if the product can be made by a method other than that recited in the base method claim." In the present situation, the method of claim 20 does not include every limitation of the claim from which it depends (i.e., claim 7) because claim 20 does not require performing the method steps recited in claim 7 for identifying at least one human coding region / gene.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 20, 25-27 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Breadth of the Claims:

The claims are drawn broadly to method for identifying a human coding region/gene including mutated and polymorphic variants thereof which are associated with any mood disorder or any related disorder, comprising identifying the position of a coding region or gene between the markers D18S68 and D18S979 that can be compared to an "equivalent region" in a person afflicted with a mood disorder or a related disorder, and detecting differences in the coding region or gene of said individual wherein a difference in the coding region or gene or an equivalent region identifies a coding region or gene or mutated or polymorphic variant associated with the mood disorder or related disorder. The claims further include variations of the method

stated above in which a nucleotide triplet within the region between D18S68 and D18S979 is detected as a means for identifying a human coding region/gene including mutated and polymorphic variants thereof which are associated with any mood disorder or any related disorder. Claims 25-27 and 29 encompass determining the susceptibility of an individual to a mood disorder or related disorder by detecting a polymorphism in the region between the markers D18S68 and D18S979 that is different in an individuals sample and a control sample as indicative of the presence of a susceptibility to a mood disorder or related disorder.

Accordingly, the claims broadly encompass diagnosing any of a large multitude of mood disorders or any disorder that is in any way related to a mood disorder. As set forth on page 1 of the specification, "mood disorder or related disorder" encompasses any mood disorder (bipolar I, bipolar II, depression), schizophrenia and "related disorders," anxiety disorders, adjustment disorders and personality disorders. Thereby, the claims encompass detecting genes associated with and diagnosing a wide variety of psychiatric disorders having varying etiologies and symptomologies. The claims also encompass detecting any human coding region or gene, wherein in the gene or coding region and mutated and polymorphic variants thereof are not defined in terms of any structure or functional properties. The claims do not define the coding region or gene to be identified, or any mutations or variants that are to be identified. The claims as broadly written encompass methods of searching for known or unknown coding regions and genes and for mutations and polymorphisms in the 9.8cM region between the markers D18S68 and D18S979 and trying to establish a correlation between these

regions/genes, mutations and polymorphisms and the occurrence of any mood disorder or related disorder. Additionally, the claims encompass detecting differences in the region between D18S68-D18S979 or D18S60-D18S61 and "equivalent regions" of an individual afflicted with a disorder. The specification does not specifically define what is encompassed by "equivalent regions." Accordingly, such regions have been interpreted as encompassing regions having some unstated degree of similar sequence and similar location in the genome as the regions flanked by the D18S68-D18S979 or D18S60-D18S61 markers.

Nature of the Invention

The claims encompass methods of diagnosing a mood disorder or a related disorder and methods for detecting a coding region or gene by assaying for the presence of genetic variation between markers D18S68 and D18S979. The invention is in a class of inventions which the CAFC has characterized as 'the unpredictable arts such as chemistry and biology" (Mycolgen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Federal Circuit 2001)).

Teachings in the Specification and State of the Art:

The specification teaches that a susceptibility locus for bipolar disease had been previously identified within the region of 18q21-q23 (page 4). The specification (page 24-25) provides the results of a study from a Belgian family (MAD31) having a BPII proband wherein the susceptibility locus was refined to include a region of 8.9 cM located between the 18q markers D18S68 to D18S979. It is stated that this region may

now be "used to locate, isolate and sequence a gene or genes which influences psychiatric health and mood" (page 5). Further, "once candidate genes have been identified it is possible to assess the susceptibility of an individual to a mood disorder or related disorder by detecting the presence of a polymorphism associated with the mood disorder or related disorder in such genes."

The specification teaches multi-linkage analysis of STRs located between the markers of D18S51 and D18S61 for cosegregation with bipolar disease in family MAD31. The results of LOD score analysis is set forth in Table 2 (page 31). The highest individual LOD score obtained for any marker was 2.01. However, as set forth on page 4 of the specification, "A LOD score of 3 (or likelihood ratio of 1000 or greater) is taken as significant statistical evidence for linkage."

The specification does not disclose a single gene or coding region within the region of D18S68-D18S979. Further, the specification does not disclose any particular mutations or polymorphisms within the region of D18S68-D18S979 which are associated with BP or any other mood related disorder. Moreover, the specification does not provide any results regarding the linkage of the D18S68-D18S979 markers or other markers within this region and the occurrence of other mood related disorders, such as schizophrenia, panic disorder, adjustment disorders or personality disorders.

The Predictability or Unpredictability of the Art and Degree of Experimentation:

The art of identifying genes associated with a disease and detecting the presence of novel mutations associated with the occurrence of disease is highly

unpredictable. Once a region associated with a gene is known, extensive experimentation remains to determine which, if any, genes within this region are sufficiently linked to a disease in order to allow for diagnosis of the disease by detecting the gene. Further, once a gene associated with a disease is identified, significant experimentation is also required to identify particular mutations and polymorphisms within that gene which are diagnostic of disease. The identity of the gene/coding region and the identity of the mutations and polymorphisms are the novel features required to practice the claimed invention. However, the specification does not teach the structural and functional properties of the coding regions/genes or mutations/polymorphisms. Rather, the specification outlines the methodology by which a researcher could perform extensive, trial-by-error experimentation in order to try to identify genes/coding regions and mutations/polymorphisms which could be used within the claimed methods. Disclosure of a 8.9 cM region linked to BPII is not equivalent to disclosing specific genes/coding regions and nucleotide variations which are associated with BP or other mood related disorders. To identify genes or mutations within this 8.9 cM region requires significant experimentation in which researchers may be required to create a clonal library containing candidate cDNAs which would then be sequenced and compared to nucleic acid databases to identify a gene or genes which may constitute the bipolar susceptibility gene. The cDNAs identified that map to the minimal candidate region would then used as probes to screen a contig library. This screening then identifies new markers which are used to genotype the linkage disequilibrium sample. The cDNAs identified by these screens are then used to screen patient DNA for

mutations and polymorphisms associated with bipolar disorders. Such random, trial-by-error experimentation is considered to be undue.

The art corroborates the unpredictability in identifying polymorphisms and mutations associated with BP and in identifying a specific loci within chromosome 18 that is definitively associated with BP. For example, McInnes (Proceedings of the National Academies of Sciences, USA. November 1996. 93: 13060-13065) teaches that interpreting results form linkage analysis of bipolar mood disorder and other behavioral phenotypes is very difficult and often misleading because behavioral phenotypes are difficult to define, as they are etiologically heterogeneous and there is a lack of knowledge as to the mode of transmission of these diseases. McInnes concluded that it is unlikely that any one linkage study will yield sufficient evidence to localize a gene for any psychiatric disorder (page 13060, col. 2, paragraph 1). McInnes performed a genome screening analysis for possible genes associated with BP and found suggestive lod scores in segments 18q, 18p and 11p. McInnes teaches that genome screening is the first step of a multi-step process for identifying genes for complex traits and that several additional steps and experiments would be required to delineate a clear candidate region (page 13064, col. 2). Gerson (Neuropsychopharmacology. 1998. 18: 232-242) reviewed the progress in identifying genes associated with manic-depressive illness and concluded that while chromosome 18, and particularly the short arm of chromosome 18, is one of the best candidate locations for a bipolar susceptibility gene, and that the positive linkage results represent important progress, scientists are still a long way from demonstrating a disease mutation correlated with bipolar illness (page

239, col. 2). Nothen (Molecular Psychiatry. 1999. 4: 76-84) concluded that as late as 1999 that the data in the art supports the hypothesis that a susceptibility locus exists and may specifically exist on chromosome 18, but does not provide a reasonable expectation that polymorphisms in the region of 18q are associated with a bipolar susceptibility locus or what that locus will be. Nothen (page 82) states that "(a)ny single study will be insufficient to provide convincing proof for a susceptibility locus in a complex disease because of unknown mode of inheritance, genetic heterogeneity, and nongenetic factors."

The teachings of Lucentini (The Scientist. December 2004, page 20) further highlight the unpredictability in the art of establishing an association between a mutation/polymorphism and the occurrence of a disease or condition. As discussed by Lucentini, reproducible association studies are "few and far between." The reference reports that "when a finding is first published linking a given gene with a complex disease, there is only roughly a one third chance that studies will reliably confirm the finding. When they do, they usually find the link is weaker than initially estimated. The first finding is usually 'spurious, or it is true, but it happens to be really exaggerated, ' ...there may be no way to predict which new gene-association studies will be verified with multiple replication."

The teachings of Gossens et al (European Journal of Human Genetics, 2000; of which 2 of the present inventors are co-authors) also supports the unpredictability in the art. In this post-filing date reference, the authors report that no association was found between triplet repeats in the 18q21.33-q23 region and bipolar disease family MAD31

and 75 unrelated BP cases (see page 388). With particular respect to claims 7, 9,10, 20, 26 and 27, the specification and prior art do not teach any particular trinucleotide repeats in the regions between D18S60-18S61 or D18S68-D18S979 whose presence is indicative of a coding region or gene or mutated or polymorphic variants thereof associated with mood disorders or related disorders.

Further, it is highly unpredictable as to whether the linkage results obtained with family MAD31 would be applicable to other mood disorders or to other related disorders. The different types of mood disorders have different symptomologies and there is no known universal correlation between the genes and mutations associated with one type of mood disorder and all other types of mood disorders. The etiology and symptomology associated with bipolar disorder are further distinct from those of other types of psychiatric disorders, including schizophrenia, depression, panic disorder, anxiety disorder, personality disorders etc. No evidence or scientific arguments have been presented to establish that the results obtained with one family having a BPII proband can be extrapolated to all other types of mood disorders and "related disorders." The post-filing date art corroborates the unpredictability in extrapolating the results obtained with BPII to other psychiatric diseases. For instance, Nancarrow (American Journal of Medical Genetics. 2000. 96: 224-227) reported that there was no association between bipolar susceptibility regions on 18q or 18p and susceptibility to schizophrenia in the 43 schizophrenia pedigrees studied (page 226).

Amount of Direction or Guidance Provided by the Specification:

The specification does not provide any specific guidance as to how to predictably identify a coding region / gene or mutation / polymorphism in the D18S68-D18S979 region which is associated with and can be used to diagnose a mood disorder or a related disorder. While methods for performing linkage analysis and for sequencing genes and comparing the sequence of genes from patients and control individuals are known in the art, such methods provide only the general guidelines that allow researchers to search for novel genes and mutations. Providing methods for searching for a gene or mutation is not equivalent to teaching specific genes and mutations associated with mood disorders and related disorders. Even by following the method steps set forth in the present claims, one would not arrive at coding regions/genes or variants thereof that are associated with mood disorders. The mere presence of a genetic variation between the DNA of one affected person and the DNA of one control person does not alone indicate that the variation is associated with a disorder, since many of the variants will not be specific to the affected individuals. That is, the variants are equally likely to represent polymorphisms present in the general population and not specifically associated with a mood disorder in the general population.

The teachings in the specification do not provide a reasonable expectation that one of skill in the art can identify variants associated with bipolar mood disorder or can identify a bipolar susceptibility locus without undue experimentation because of the high level of unpredictability in the art (as discussed above) and because the specification has not provided evidence that would allow the skilled artisan to predict the location and identity of specific bipolar susceptibility genes and mutations / polymorphisms. The

specification presents data defining a smaller region of the 18q arm which has a higher probability of containing a susceptibility locus, but as of 1999, the art indicates that scientists are a long way from pinpointing specific genes, polymorphisms and mutations that are associated with bipolar disease or related disorders. The specification describes a research project for searching for genes and mutations that may exist in the defined region but the protocol described constitutes undue experimentation because the skilled artisan would be required to perform a large amount of essentially random screening of the defined region and would not be able to reasonably predict from the specification the identity of the gene or mutations associated with BP. Furthermore, the claims as written are directed to a research project without a predictable outcome because they encompass methods which detect novel bipolar disease susceptibility genes and polymorphisms. The art makes clear that this objective is of great interest and the target of extensive research by many groups. In fact, many groups have taken the same approach as described in the specification for identifying such a bipolar locus without success. The specification essentially suggests that the artisan should analyze all possible mutations or polymorphisms within the 8.9 million bp region of D18S to D18S979 and then determine which variations within this region represent mutations or polymorphisms that could be used to diagnose a mood disorder. Such experimentation is considered to be undue.

Working Examples:

The specification does not provide any working examples of methods in which a coding region / gene or mutated or polymorphic variant thereof is identified and wherein

the coding region / gene or variant is associated with mood disorder or any other related disorder.

Conclusions:

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". In the instant case, the claims do not bear a reasonable correlation to the scope of enablement because the specification does not teach a single coding region or gene or variant thereof which is associated with mood disorder or any related disorder. The specification does not provide the novel aspects of the claimed invention because the disclosure of a 8.9 cM region linked to BPII is not equivalent to teaching specific sequences that constitute coding regions / genes or mutations that are associated with BP or other mood related disorders. The specification provides the researcher with only an invitation to experiment and to try to find a new gene or mutation that is associated with mood disorder and which could be

used to diagnose mood disorder. No specific guidance is provided as to what would be the identity of such a gene or mutation / polymorphism. Accordingly, given the high level of unpredictability in the art and the lack of specific guidance provide in the specification and prior art, it would require undue experimentation for one of skill in the art to practice the claimed invention.

RESPONSE TO ARGUMENTS:

In the response, Applicants traversed the previous grounds of rejection by arguing that the LOD score need not be greater than 3 because Applicants did not perform a complete genome scan of family MAD31, but rather a fragment of chromosome 18 was scanned using STR markers in a multilocus linkage analysis. Applicants state that they have provided a copy of the Lander reference which establishes that a LOD score of 1.2, with p=0.01 is acceptable. However, Applicants did not in fact provide a copy of the cited Lander reference. Note that it is Applicant's responsibility to provide copies of the references that they cite in their response. Nonetheless, the Lander reference is not considered to support the contention that the data set forth in the specification enables the presently claimed invention. Lander states that a p-value of 0.01 "should be required to declare confirmation at the 5% level." The present specification does not appear to provide any p-values for the linkage data. Lander also states that this correction is equivalent to a multiple testing correction for 5 markers. It is further stated that "replication studies should always state their power to detect the proposed effect with the given sample size." This information is not provided in the present application and thereby the significance of the disclosed LOD scores

cannot be properly evaluated. Lander also emphasizes the fact that the size of the family and the number of families studied significantly effects the interpretation of the data. Yet, the present study was performed using only one Belgium family with a BPII proband. Further, a showing that a region of 18q is linked to BPII in family MAD31 does not provide sufficient evidence of a specific gene or variant thereof within this region that is linked with a mood disorder or related disorder, for the reasons set forth in the above rejection.

Applicants argue that the fact that Goossens teaches that the specific triplets in that study were not associated with mood disorder is not relevant because the individual repeats represent only a small region within the large region flanked by markers D18S86 and D18S979. This argument has been fully considered but is not convincing because the findings of Goossens emphasizes the unpredictability in the art. The present claims require the detection of triplet repeats as a means for identifying a coding region / gene or variant thereof associated with mood disorder. However, Goossens establishes that the triplets that they studied from this region were not associated with mood disorder. In particular, claims 7, 9 , 10, 20, 26 and 27 are drawn to methods in which the detection of any triplet between D18S69-D18S979 is detected as indicative of the presence of a coding region or gene variant thereof associated with a mood disorder. Claims 9 and 10 specifically require detection of the repeat CAG or CTG. Yet, Goossens teaches that the CAG and CTG triplets between D18S69-D18S979 are not involved in BP disorder. If these triplets are not useful for identifying genes and mutations associated with mood disorders or for directly diagnosing mood

disorders, what would be the identity of triplets that can be used for this purpose? Such teachings are not provided in the specification or in the prior art. Additionally, the teachings of Goossens highlight the need to perform random, trial-by-error experimentation in order to try to identify sequences within D18S69-D18S979 which can be used to identify genes and mutations associated with mood disorder.

Applicants further argue that the claims do not pertain to "any mood disorder." But rather "the claims are limited to identifying human coding regions / genes relevant to mood disorders." However, the claims encompass identifying at least one human coding region / gene including mutated or polymorphic variants thereof, which is "**associated with a mood disorder or related disorder**." As defined in the specification (page 1), such disorders are intended to include any disorder defined in the Diagnostic and Statistical Manual of Mental Disorders IV of mood disorders, schizophrenia and related disorders, anxiety disorders, adjustment disorders and personality disorders. The claims also include the diagnosis of these disorders. Thereby, the claims do in fact encompass the analysis of a very large and distinct genus of psychiatric disorders. Yet, the specification provides information regarding only the association between the stated 18q regions and members of a Belgium family having a BPII proband. It is further asserted that the claims are limited to specific regions of human chromosome 18q. However, the claims are not in fact limited to coding regions/genes or mutations present only in the D18S68-D18S979 region or D18S60-D18S61 region because the claims encompass the analysis of "equivalent regions." The specification does not specifically define what is encompassed by such equivalent regions. Accordingly, such regions

have been interpreted as encompassing regions having some unstated degree of similar sequence and similar location in the genome. Thereby, the claims are not considered to be limited to specific regions of human chromosome 18q.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6, and 8 are indefinite over the recitation of "equivalent regions." This phrase is not clearly defined in the specification and there is no art recognized definition for this phrase. It is not clear as to what would be the structural or functional properties of "equivalent regions." Accordingly, one cannot determine the meets and bounds of the claimed invention.

RESPONSE TO ARGUMENTS:

In the response, Applicants traversed this rejection by arguing that one would know that equivalent regions means regions occupying the equivalent physical location on chromosome 18q or the same genetic locus. It is asserted that one would know that equivalent regions has a meaning similar to homologous. However, these definitions for "equivalent" are not provided in the specification and are not definitions known in the art to define "equivalent" nucleic acid regions. In fact, regions having equivalent physical locations are distinct from regions which share sequence homology since sequences may be translocated to other locations within a chromosome or to other chromosomes,

without altering the homology or identity of the sequence. It is also unclear as to whether an equivalent physical location would require that the sequence be at the exact location or if this includes some variation in the physical location of the regions. It is further unclear as to whether homologous regions share 100% sequence identity or may share other, undefined levels of sequence identity (99%, 90%, 80%, 50% etc). Accordingly, because the specification does not clearly define what is intended to be encompassed by equivalent regions and because there is no art fixed definition for this phrase, it is maintained that the artisan would not be able to determine the meets and bounds of the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571)-272-0745.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

Carla Myers
April 6, 2005

CARLA J. MYERS
PRIMARY EXAMINER